REMARKS

Claims 1-35 are currently pending in the application. Claims 1 and 31 have been amended. Support for the amendment to claims 1 and 31 is found at page 17, lines 29-31. Applicants respectfully assert that no new matter has been added and request reconsideration of the claims currently pending in the application.

On page 3 of the Office Action, claims 1-2 and 7-35 are rejected under 35 U.S.C. § 112 first paragraph as failing to comply with the written description requirement. The Applicants respectfully traverse this rejection.

The Examiner asserts that the specification of this application does not contain an adequate description for the entire scope of the terms in the claims such as "stimulation compound". The Examiner then cites Eli Lilly, 119 F.3d at 1568.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one of skill in the art can reasonably conclude that the inventor had possession of the claimed invention. MPEP § 2163 I.

As discussed in § 2163 II.A.3.(a).ii, the written description requirement may be satisfied in many ways. One way is to determine whether the application describes an actual reduction to practice of the claimed invention. In the present application, a specific stimulation compound (HIF-1) is described.Og As also explained in § 2163 II.A.3.(a).ii , functional recitation may be sufficient. Claims 1 and 31 have been amended to better describe the mechanism for stimulation of production of VEGF (claim 1) and growth factors (claim 31) in functional terms. Claim 1 now states that the stimulation compound activates an enhancer/hypoxia response element for production of VEGF. Claim 31 states that the stimulation compound activates an enhancer/hypoxia response element.

The written description requirement may be satisfied through disclosure of function and minimal structure when there is a well-established correlation between structure and function. MPEP § 2163 II.A.3.(a).ii. In the instant application, claim 1 as amended, describes the function (stimulation) of production of VEGF through a structural description (activation of an enhancer/hypoxia response element). Likewise, claim 31 describes function (stimulation) of production of grow factors through a structural description (activation of an enhancer/hypoxia response element. U.S. Patent No. 6,124,131 cited in this application and incorporated by reference describes hypoxia response in great detail.

Regarding Eli Lilly, this was a case in which the specification provided only a general method of producing human insulin cDNA and the description of the human insulin A and B amino acid sequences that cDNA encodes. It did not provide a written description of the cDNA. Accordingly, claim 5 of the patent under consideration in Eli Lilly was held invalid for failure to provide an adequate written description. This is not the situation in the instant application. The instant application includes a very specific description of a species of the stimulation compound and how the stimulation compound functions with respect to structure. Therefore, the applicants were in possession of the claimed invention and the written description is adequate in view of the amended claims. Removal of the rejection under 35 U.S.C. § 112, first paragraph is respectfully requested.

If the Examiner continues to believe that claims 1-2 & 7-35 fail to comply with the written description requirement, then the Examiner is requested to be more specific as to what is lacking.

Rejections under 35 U.S.C. § 102

Carlyle, et al. WO 99/37337

On page 4 of the Office Action, claims 31-35 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Carlyle, et al. (WO 99/37337). Applicants respectfully traverse the rejections.

The Examiner states that "Carlyle, et al. teaches a substrate, e.g. a prosthesis, on which is coated VEGF or related factors. The factors are attached via chemical bonding, crosslinking or an adhesive. The reference anticipates the claimed subject matter."

To anticipate a claim, the reference must teach every element of the claim. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). Therefore, all claim elements, and their limitations, must be found in the prior art reference to maintain a rejection based on 35 U.S.C. § 102. Applicants respectfully submit that Carlyle, et al. does not teach every element of claims 31-35, and therefore fails to anticipate claims 31-35.

Carlyle, et al. teach that VEGF is joined with a substrate by direct contact in solution or alternatively that VEGF can be joined with the substrate either through application to the substrate along with a binder or through chemical binding of the VEGF to the substrate. There is absolutely no teaching or suggestion in Carlyle, et al. of associating a stimulation compound with a biocompatible material to stimulate the production of growth factors. The Examiner also acknowledges this on page 6 of the Office Action in rejecting claims 1-35 under 35 U.S.C. § 103 (a) as being unpatentable over Carlyle, et al. in view of Martin, et al. On page 6, the Examiner states that the reference (Carlyle, et al.) teaches all of the claimed limitations except that the reference uses VEGF and does not teach using a VEGF stimulation compound . . .". It is not understood how the Examiner can take this inconsistent position. For the Examiner to maintain a rejection under 35 U.S.C. § 102 (b), the reference must teach each and every element of the claim. It is clear that it does not. Carlyle, et al. does not teach the use of a stimulation compound. The growth factor of Carlyle, et al. is associated with the prosthesis by direct contact , the use of a binder or through chemical bonding to the substrate. If the Examiner believes otherwise, it is respectfully requested that the Examiner point out by page and line number where Carlyle, et al. teaches the use of a stimulation compound to stimulate the production of a growth factor such as VEGF.

Applicants respectfully request withdrawal of the rejection of claims 31-35 under 35 U.S.C. § 102 (b) as being anticipated by Carlyle, et al.

Keogh U.S. Patent No. 6,033,719

On page 4 of the Office Action, claims 31-33 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Keogh (U.S. Patent No. 6,033,719). Applicants respectfully traverse the rejections.

The Examiner alleges that Keogh teaches a device on which is coated a biomolecule factor through covalent bond.

Applicants respectfully disagree with the Examiner's interpretation of the Keogh patent. The Keogh patent describes an improved method for attaching a biomolecule to a substrate surface. Specifically, it is a method of covalently attaching the biomolecule. Col. 2, lines 30-34. There is no suggestion or disclosure of production of the biomolecule. What Keogh discloses is a new method of attachment.

The present invention claims a method in which a stimulation compound with a biocompatible material is used to stimulate the production of growth factors. To maintain a rejection under 35 U.S.C. § 102 (b), the reference must teach every element of the claim. There is absolutely no teaching in the Keogh patent of associating a stimulation compound with a biocompatible material for the production of growth factors. If the Examiner disagrees, it is respectfully requested that the Examiner please indicate by column and line number where in Keogh this teaching appears.

Applicants respectfully request withdrawal of the rejection of claims 31-33 under 35 U.S.C. § 102 (b) as being anticipated by Keogh.

Martin, et al. WO 98/20027

On page 5 of the Office Action, claims 1-2, 7, 23-24, 26, 28, 31-33 and 35 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Martin, et al. (WO 98/20027). Applicants respectfully traverse the rejection.

The Examiner alleges that Martin, et al. teach a device onto or into which a VEGF agonsit [agonist] is attached (see for example the claims).

On page 5 of the Office Action, claims 1-2, 7, 23-24, 26, 28, 31-33 and 35 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Martin, et al. (WO 98/20027). Applicants respectfully traverse the rejections. Applicants respectfully disagree with the Examiner's interpretation of Martin, et al. Martin, et al. describe the delivery of VEGF and an equivalent agent such as an agonist of VEGF receptors via the adventitial surface of a blood vessel. An agonist, as noted in Martin, et al. is a molecule which binds to a receptor to which VEGF normally binds and has substantially the same effects as VEGF would have. See page 10, lines 25-26. Thus, a VEGF agonist functions like VEGF and takes the place of VEGF.

On the other hand, the subject matter of independent claims 1 and 31 is directed to a stimulation compound that stimulates the production of growth factors like VEGF that activates an enhancer/hypoxia response element for the production of VEGF. This element of applicant's claims is not found in the teachings of Martin, et al. Martin, et al. is directed to VEGF or its agonists for use in suppressing intimal hyperplasia in situations wherein intimal hyperplasia arises when the endothelium is wholly or largely intact. Consequently, Martin, et al. teach a different invention and do not teach each and every element of applicant's claims. Therefore, Martin, et al. fails to anticipate independent claims 1 and 31, and their respective dependent claims 2, 7, 23-24, 26, 28, 32 and 35. If the Examiner believes otherwise, it is requested that the Examiner point out by page and line number.

Applicants respectfully request withdrawal of the rejection of claims 1-2, 7, 23-24, 26, 28, 31-33, and 35 under 35 U.S.C. § 102 (b) as being anticipated by Martin, et al.

Slaikeu, et al. WO 01/03607

On page 5 of the Office Action, claims 31-33 are rejected under 35 U.S.C. § 102 (a) as being anticipated by Slaikeu, et al. (WO 01/03607). Applicants respectfully traverse the rejections.

The Examiner alleges that Slaikeu teaches a medical device on which it is coated or associated angiogenic factor.

Slaikeu, et al. disclose a stent coated with a composition having an angiogenic response. See page 7, lines 13-23. A long list of angiogenic factors including a growth factor, a nucleic acid, a pharmaceutically active compound and so on is listed, as long as it produces the required angiogenic response. See page 11, line 8 to page 13, line 29. Slaikeu, et al. produce no teaching of a stimulation compound in association with production of VEGF, and specifically, a stimulation

compound that actives an enhancer/hypoxia response element. Therefore, Slaikeu, et al. teach a different invention and do not anticipate claim 1 because Slaikeu, et al. do not teach every element of the claim. If the Examiner still believes that the claims are anticipated, it is respectfully requested that the Examiner point out by page and line number where Slaikeu, et al. teach a stimulation compound as defined in claims 31-33.

Applicants respectfully request withdrawal of the rejection of claims 31-33 rejected under 35 U.S.C. § 102 (a) as being anticipated by Slaikeu, et al.

Rejections under 35 U.S.C. § 103

On page 6 of the Office Action, claims 1-35 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Carlyle, et al. in view of Martin, et al. Applicants respectfully traverse the rejections.

Three criteria must be met to establish a *prima facie* case of obviousness. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success. Finally, the prior art reference, or combination of references, must teach or suggest all the claim limitations. MPEP § 2142. Applicants respectfully traverse the rejection since the prior art fails to disclose all the claim limitations and there would be no motivation to combine the references as proposed by the Examiner.

The Examiner alleges that Carlyle, et al. teach the use of VEGF which has been attached to promote population of the device with viable cells and other positive results but that Carlyle, et al. describes use of VEGF and does not teach using a VEGF stimulation compound. The Examiner then further alleges that at the time the invention was made to substitute a VEGF stimulation compound for the VEGF used by Carlyle, et al. was obvious because Martin, et al. teach that using such compounds produces like results to using the peptide itself.

Applicants respectfully disagree. As discussed above, Carlyle, et al. teach that VEGF is joined with a substrate by direct contact or alternatively that VEGF can be joined with the substrate either through application to the substrate along with a binder or through chemical binding of the VEGF to the substrate. Carlyle, et al. do not teach the use of a stimulation compound to stimulate the production of VEGF, especially, the type of stimulation compound as is now defined in independent claims 1 and 31. Carlyle, et al. broadly teaches associating growth factors with substrates to stimulate cell growth and specifically teaches in its examples the attachment of isolated growth factors onto substrates.

Martin, et al. on the other hand discloses a therapeutic use of growth factors that is to suppress intimal hyperplasia. Page 1, lines 4-6 and page 4, lines 25-29. Additionally, Martin, et al. teach that VEGF agonists can be used in practicing their invention and that VEGF agonists function like VEGF and may take the place of VEGF. See page 10, line 22 to page 13, line 17. Similarly Carlyle, et al. and Martin, et al. do not teach the use of a stimulation compound. Therefore, it is not understood how the combination of Martin, et al. and Carlyle, et al., if such combination could even be made, teaches the use of stimulation compounds as now defined in amended claims 1 and 31 and their respective dependent claims. Therefore, the combination of Carlyle, et al. and Martin, et al., assuming such combination can be made, do not teach or suggest all of the claim limitations, and specifically, the use of a stimulation compound. Applicants respectfully request withdrawal of the rejection of claims 1-35 under 35 U.S.C. § 103 (a) as being anticipated by Carlyle, et al. in view of Martin, et al.

On page 7 of the Office Action, claims 3-7 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Carlyle, et al. in view of Martin, et al. and further in view of Semenza, et al. (U.S. Patent No. 6, 124,131) or Tsuzuki, et al. (Cancer Research. 60.2000). Applicants respectfully traverse the rejections.

The Examiner asserts that neither Carlyle, et al. nor Martin, et al. specifically teach using HIF-1α as the stimulator/agonist of VEGF, however, it would have been obvious at the time the invention was made to use HIF-1α as the agonist as taught by Martin, et al. in the process of Carlyle, et al. because Semenza and Tsuzuki teach that HIF-1α is a known agonist of VEGF. The Examiner then makes the statement there was reasonable expectation that substituting HIF-1α for the VEGF in the invention of Carlyle, et al. would produce like results.

However, in establishing a case of obviousness, first there must be some suggestion or motivation either in the references themselves or in the knowledge generally available to one of ordinary skill in the art to combine the reference teachings. Again, as discussed in relation to the 35 U.S.C. § 103 (a) rejection based on the combination of Carlyle, et al. and Martin, et al., there is absolutely no motivation or teaching to combine those two references. Carlyle, et al. generally teach that growth factors can promote cell growth while Martin, et al. teach that VEGF and its agonists can suppress or treat stenosis. Neither reference teaches or suggests the use of a stimulation compound, especially one that as now defined in amended independent claim 1. Therefore, the Examiner's assertion that Semenza and Tsuzuki teach that HIF-1α is a known agonist of VEGF is not understood as how that could be some suggestion or motivation to use an agonist as a stimulation compound. It is respectfully requested that the Examiner clarify his position by documenting how an agonist can function as a stimulation compound, especially as the stimulation compound as now defined in amended independent claim 1.

As applicants discuss in their response mailed on January 5, 2003, Semenza teaches the discovery in isolation of unique variant forms of HIF-1α and Ts0uzuki, et al. attempt to quantify the activation of VEGF promoter by implanting VEGF and stem cells in mice. The Examiner is requested to identify where in the four references cited is there the suggestion or motivation to make the combination.

Furthermore, even if the combination could be made, there is no reasonable chance of success. As discussed previously, an agonist is not a stimulation compound that stimulates the growth of VEGF, but only a VEGF look-a-like. Therefore, the Examiner's suggestion of reasonable expectation of success is not tenable.

In view of the above, applicants respectfully request withdrawal of the rejection of claims 3-7 under 35 U.S.C. § 103(a) as being anticipated by Carlyle, et al. in view of Martin, et al. and further in view of Semenza, et al. or Tsuzuki, et al.

In view of the amendments and reasons provided above, it is believed that all pending claims are in condition for allowance. Applicants respectfully request favorable reconsideration and early allowance of all pending claims.

If a telephone conference would be helpful in resolving any issues concerning this communication, please contact Applicants' attorney of record, Hallie A. Finucane at (612) 334-3222.

The Director is authorized to charge any fee deficiency required by this paper or credit any overpayment to Deposit Account No. 23-1123.

Respectfully submitted,

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